Reviewer's report

Title: Simultaneous copy number gains of NUPR1 and ERBB2 predicting poor prognosis in early-stage breast cancer

Version: 1 Date: 28 January 2012

Reviewer: Yeul Hong Kim

Reviewer's report:

The authors identified chromosomal alterations associated with poor prognosis in early-stage breast cancers (EBC). They analyzed copy number alterations in 48 frozen tissues gDNA of EBC (discovery set) using 30K whole-genome human oligoarrays and validated the recurrently altered regions (RARs) in 97 formalin-fixed, paraffin-embedded tissues of EBC (replication set) using Real-Time PCR. A total of 23 RARs were defined in the discovery set and among the 23 RARs, copy number gains on 16p11.2 (NUPR1) and 17q12 (ERBB2) showed significant associations with poor prognosis. Also, in the independent replication, double-positive for NUPR1-ERBB2 gains showed a highly significant association with poor prognosis in multivariate analysis. This study is quite valuable to identify a potential prognostic biomarker for the early breast cancer. This work may contribute to the understanding of Breast cancer carcinogenesis and support the development of important diagnostic biomarker. However, there are some minor concerns that need to be addressed and clarified before this paper can be published.

Minor Essential Revisions;

1. Authors described that gDNA from a healthy female was used as normal reference for all array-CGH experiments. But, more information is needed.

2. The authors identified that simultaneous gains of NUPR1 and ERBB2 can be a significant predictor of poor prognosis in EBCs. However, the NUPR1 gain was not replicated in the larger replication set. This result need to be discussed. What might be the reason of failure of replication? Is there any possible explanation for cross activity between NUPR1 and ERBB2 gene function?

3. In discussion, authors stated that “Of the RARs identified in this study, 15 RARs were commonly detected in both stages I and II, which suggests that these copy number alterations are acquired at an earlier stage including precancerous stage.”. However, precancerous stage samples were not tested in this experiment. This description should be limited in stage I and II EBC.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the
statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.